

REMARKS

Claims 1-12, 40-51, 53-56, 77-83, and 85-92 are now pending in the application. The Examiner is respectfully requested to reconsider and withdraw the rejections in view of the amendments and remarks contained here.

REJECTION UNDER 35 U.S.C. § 112

Claim 54 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. This rejection is respectfully traversed. Applicants have amended Claim 54 to depend on Claim 53. Accordingly, reconsideration and withdrawal of the present rejection are respectfully requested.

Claims 1-12, 40-52 and 78-92 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. This rejection is respectfully traversed. Applicants direct the Examiner's attention to at least Paragraphs [0005] and [0006] and discussed in the examples [0032]-[0048] for support for the use of "a first plurality of genes" and "a second plurality of genes." The terms "first" and "second" were added by Applicants to provide clarity and precision to the claims (MPEP §§ 2173.02 and 2173.05(e)) and not to overcome any cited art. As stated in the cited MPEP sections, "a claim term that is not used of defined in the specification is not indefinite if the meaning of the claim term is discernible." *Bancorp Services, L.L.C. v. Hartford Life Ins. Co.*, 359 F.3d 1367, 1372, 69 USPQ2d 1996, 1999-2000 (Fed. Cir. 2004). Furthermore, "[t]here is no requirement that the words in the claim must match those used in the specification disclosure. Applicants are given a great deal of latitude in how they choose to define their invention so long as the terms and phrases used define

the invention with a reasonable degree of clarity and precision.” However, in an effort to expedite prosecution, Applicants have amended Claims 1-12, 40-52, and 78-92 by removing the terms “first” and “second.” Accordingly, reconsideration and withdrawal of the present rejection are respectfully requested.

REJECTION UNDER 35 U.S.C. § 103

Claims 1-12, 40-52, and 77-92 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Gordon et al., (US Patent Publication 2003/0219760, August 30, 2002) in view of Alizadeh et al., (Nature, Vol 403, page 503-511, February 2000), Rocke et al., (US Patent Publication 2002/0111742, August 15, 2002), Robetorye et al., (J of Molecular Diagnostics, Vol 4, page 123-126, August 2002), de Vos et al., (Lab Invest, Vol 83, page 271-285, February 2003) and Goldberg et al., (US Patent Publication 2003/0060439, January 11, 2001). This rejection is respectfully traversed.

At the outset, Applicants respectfully submit the originally filed claims are patentably distinct over the cited reference. However, in an attempt to expedite prosecution, Applicants have amended Claim 1 to include said plurality of genes predictive of the patient having DLBCL. In contrast, Gordon, Alizadeh, Rocke, Robetorye, de Vos, and Goldberg, individually or in combination, do not teach or suggest a method for classifying if a patient having DLBCL, the method comprising providing a plurality of primers designed to hybridize to a plurality of genes in a tumor sample of a patient, said plurality of genes predictive of a patient having DLBCL and amplifying said plurality of genes using said plurality of primers. Applicants submit that the Examiner has failed to establish a *prima facie* case of obviousness as required by

Graham v. John Deere Co., 148 USPQ 459 (1966) and MPEP § 2141. Specifically, the following tenets of patent law must be adhered to:

- (A) The claimed invention must be considered as a whole;
- (B) *The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination;*
- (C) *The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention;* and
- (D) Reasonable expectation of success is the standard with which obviousness is determined.

MPEP § 2141.01

There is no teaching, suggestion, or motivation set forth in Gordon, Alizadeh, Rocke, Robetorye, de Vos, and Goldberg, to combine these references to produce the claimed invention. It is readily apparent that neither Gordon, Alizadeh, Rocke, Robetorye, de Vos, nor Goldberg, provide any teaching, suggestion, or motivation clearly found within the text of these references, it is improper to combine these references to establish a rejection of obviousness unless the Examiner can show a teaching, suggestion, or motivation is generally available in the knowledge of one skilled in the art.

A statement that a modification is well within the skill in the art is not sufficient by itself to establish *prima facie* obviousness. The Examiner simply picks and chooses among the elements that allegedly teach the claimed invention. However, the Examiner has failed to show any motivation within these references to make such a combination.

As appropriately stated in MPEP § 2143.01, “[a] statement that modification of the prior art to meet the claimed invention would have been well within the ordinary skill of the art at the time the claimed invention was made the references relied upon teach that all aspects of the claimed were individually known in the art is not sufficient to establish a

prima facie case of obviousness without some objective reason to combine the of the references.” *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993)(emphasis in original); MPEP § 2143.01. That is, it is the burden to identify some objective reason to combine the teachings of the references. However, as stated above, the Examiner merely indicated that combinations were “obvious to one of ordinary skill in the art.” Therefore, Applicants respectfully request the Examiner to identify some suggestion or motivation, either in references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify or combine reference teaching.

Since, at this time, the Examiner has failed to provide any objective evidence found in the references to support the combination of these references, the Examiner must present a convincing line of reasoning as to why one skilled in the art would have combined these references. According to MPEP § 2142, it is the Examiner’s initial burden to provide some suggestion of the desirability of doing whatever the inventor has done. Specifically, “[t]o support the conclusion that the claimed invention is directed to obvious subject matter, either the references must expressly or impliedly suggest the claimed invention or the examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references.” *Ex parte Clapp*, 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985).

Gordon fails to provide any disclosure as to RT-PCR for measuring gene expression from a tumor sample from a patient having DLBCL and one skilled in the art would need undue experimentation to invent the claimed invention. Gordon does not teach RT-PCR for DLBCL patients in paragraphs 84 and 93 but rather use RT-PCR to confirm gene expression from micro array analysis of those patients with mesothelioma and breast cancer, respectively, but not

DLBCL. In addition, Applicants respectfully disagree with the Examiner that Gordon teaches an internal control of GAPDH as a housekeeping gene for PCR. As quoted by Gordon in paragraph 182, “hybridization of RNA to high density polynucleotide micro arrays prior to hybridization to experimental raise the quality of the cRNA was assessed for approximately half of all samples using test arrays designated to compare relative expression levels of β -actin and GAPDH by using ocleonucleotide probes.” Gordon teaches the use of a control GAPDH for micro array analysis and not for PCR. Gordon does not teach or suggest a method of RT-PCR in correlation and normalization of the expression of the plurality of genes being predictive of a patient having DLBCL. Robetorye and de Vos, individually or in combination, fail to teach or to suggest a method for classifying a patient with DLBCL but rather suggest that expression data analyzed using micro arrays may be confirmed by RT-PCR. In the absence of any objective evidence or any convincing line of reasoning to combine these references, Applicants respectfully submits that each of the references, individually or in combination, fail to teach or to suggest the claimed invention. Thus, the Examiner has failed to establish a *prima facie* case of obviousness. Accordingly, reconsideration and withdrawal of the present rejection are respectfully requested.

Furthermore, Gordon, Alizadeh, Rocke, Robetorye, de Vos, and Goldberg, individually or in combination, fail to teach or to suggest a kit comprising an assay for measuring expression of the plurality of genes in a tumor sample from a patient having DLBCL, the assay comprising a plurality of primers designed to hybridize a plurality of genes in the tumor sample from a patient having DLBCL, a database comprising normalized reference values as reference values of a plurality of genes, and an algorithm for determining which at least are of a plurality of classification groups includes the patient having DLBCL. Applicants respectfully disagree with the Examiner as to the Examiner’s assessment of Gordon. Gordon teaches “kits for cancer

diagnosis. The kits include a set of one or more ratios applicable to the analysis of gene expression data, wherein the ratio is calculated from the expression levels of at least one upregulated gene that is expressed in greater amounts in the cancer cells than in corresponding non-cancer cells and at least one down regulated gene that is expressed in lesser amounts in cancer cells than in corresponding non-cancer cells. In certain embodiments, the kit also includes instructions for the use of the one or more ratios in the diagnosis of the presence of cancer cells in a biological sample.”

Applicants submit that the Examiner has failed to establish a *prima facie* case of obviousness as required by *Graham v. John Deere Co.*, 148 USPQ 459 (1966) and MPEP § 2141. Gordon, individually or in combination with any of the cited references, does not provide enabling disclosure as to a kit measuring gene expression of a plurality of genes from a tumor from a patient having DLBCL and one skilled in the art would need undue experimentation to invent the claimed invention as discussed above. None of the above cited references suggest a kit comprising a database. For a claim to be obvious, each and every element of the claim must be taught in the prior art. The Examiner has failed to establish a *prima facie* case of obviousness. Accordingly, reconsideration and withdrawal of the present rejection are respectfully requested.

Moreover, Gordon, Alizadeh, Rocke, Robetorye, de Vos, and Goldberg, individually or in combination, fail to teach or to suggest a method to determine the survival probability of a patient diagnosed with DLBCL, a method comprising amplifying a first plurality of genes from a patient diagnosed with DLBCL, measuring expression for said first plurality of genes, normalizing expression for said plurality of genes to produce normalized expression values in correlating said normalized expression values of said plurality of genes to data ratified to the classification groups to determine the probability of survival of the patient

diagnosed with DLBCL. As discussed above, neither Gordon, Robetorye, nor de Vos, individually or in combination, provide an enabling disclosure for such a method and one skilled in the art would need undue experimentation to invent the invention. In addition, there is no teaching, suggestion, or motivation set forth in the cited references to combine these references to produce the claimed invention. “Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in references themselves or in the knowledge generally available to one of ordinary skill in the art.” MPEP § 2143.01 (emphasis added); *In re Fine*, 5 USPQ2d 1596 (Fed Cir 1988). A statement that a modification is well within the skill in the art is not sufficient by itself to establish *prima facie* obviousness. Accordingly, reconsideration and withdrawal of the present rejection are respectfully requested.

ALLOWABLE SUBJECT MATTER

The Examiner states that Claim 54 would be allowable by resolution of the § 112 second paragraph issues changing the dependence. Accordingly, as discussed above, Applicants have amended Claim 54 to depend on Claim 53 instead of Claim 52. Therefore, Claim 54 should now be in condition for allowance.

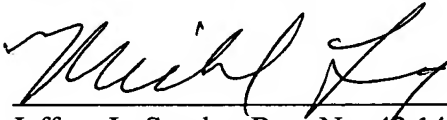
Any claim amendments not discussed above are merely grammatical corrections or to add precision and clarity to the claim and not to overcome any of the cited references. Therefore, the amendments are entitled to their full range of equivalence.

CONCLUSION

It is believed that all of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants, therefore, respectfully request that the Examiner reconsider and withdraw all presently outstanding rejections. It is believed that a full and complete response has been made to the outstanding Final Office Action and the present application is in condition for allowance. Thus, prompt and favorable consideration of this amendment is respectfully requested. If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (248) 641-1600.

Respectfully submitted,

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